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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/548,403

07/27/2006

Marie Bendix Hansen

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EXAMINER

KIM, ALEXANDER D

ART UNIT

PAPER NUMBER

1656

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/548,403	<b>Applicant(s)</b> HANSEN ET AL.	
	<b>Examiner</b> ALEXANDER D. KIM	<b>Art Unit</b> 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 14 December 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>09/08/2005, 07/27/2006</u> .                                  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Application Status***

1. In response to the previous Office action, a written restriction requirement (mailed on 10/15/2007), Applicants filed a response received on 12/14/2007. Claims 1-15 are pending in this instant Office action.

### ***Election***

2. Applicant's election with traverse of species (i.e., proteins in claim 6, lactoferrin in Claim 7, body fluids in Claim 8 and milk in Claim 9) in a paper filed on 12/14/2007 is acknowledged. The previous requirement of species election on Claim 6 (mailed out on 12/14/2007) has been withdrawn by virtue of Applicants' argument and reconsideration by the Examiner. The traversal is on the ground(s) that the Markush group occurs in a claim reciting a process, then it is sufficient if the members of the group are disclosed in the specification to possess at least one property in common which is responsible for their function in the claimed relationship, and it is clear from their very nature or from the prior art that all of them possess this property. Applicants also argue there is no serious burden to examine all species because of their very nature possess in common among species. This is not found persuasive because each species in Claims 7-9 are not so closely related to each other because of their distinct structural features and/or their functional relationship; thus, lacks the unity of invention. Also, each species require a distinct key word(s) search in the database. Searching all together is burdensome because once one species is searched, not all the individual species have also been

searched; thus, search burdensome for searching all species in Claims 6-9. The requirement is still deemed proper and is therefore made FINAL.

Claims 1-15 are pending in the instant application and will be examined herein.

### ***Priority***

3. The instant application is a 371 filing of the International Application No. PCT/DK04/00187 filed on 03/19/2004. The Examiner notes that the requirements of national stage entry of the instant application had been completed (note assigned U.S. filing date) within 30 months of the earliest claimed priority date; the related international application includes both a search report and a preliminary examination report.

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) to a foreign patent application 2003 00443 (Denmark) filed on 03/21/2003 in English.

### ***Information Disclosure Statement***

4. Information disclosure statements (IDS) filed on 07/27/2006 and 09/08/2005 have been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

### ***Claim Objections***

5. Claims 2-3 and 14-15 are objected to because of the following informalities:

Claims 2-3 and 14-15 recite symbol "I". The use of abbreviation "I" should be spelled out on a first appearance in claims. Appropriate correction is required.

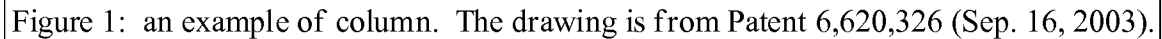
***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-15 are rejected under of 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claim 1 (Claims 2-15 dependent therefrom) recites the limitation "a linear flow rate of at least 1.500 cm/hour". The recited limitation of a linear flow rate is a relative term which renders the claims indefinite because a linear flow rate represented by cm/hour can be varied depending on a place of measurement in the chromatography system. For example, the linear flow rate at point A is slower than point B in Figure 1, as shown below. Appropriate clarification is required.



### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 5-10 and 12-15 are rejected under 35 U.S.C. 102(b) as anticipated by Kawakami et al. (US Patent 4,997,914, Mar. 5, 1991) as evidenced by Hirai et al. (US Patent 6,475,478, Nov. 5, 2002), Mitoma et al. (The Journal of Biological Chemistry, volume 276, pages 18060-18065) and Yashida et al. (Biotechnology and Bioengineering, 1994, volume 43, pages 1087-1093).

Claim 1 is drawn to a process for isolation of one or more bio-molecule(s) from a bio-molecule-containing fluid comprising the steps of: a) optionally adjusting the pH of the bio-molecule-containing fluid; b) bringing the bio-molecule-containing fluid to a temperature of at least 40°C; c) applying a volume of said bio-molecule-containing fluid having a temperature of at least 40°C to an expanded bed adsorption column comprising an adsorbent, said expanded bed column is operated with a linear flow rate of at least 1.500 cm/hour; d) optionally washing the column; e) eluting at least one bio-molecule from the adsorbent. Claims 5-9 and 12-15 are drawn to a process of Claim 1 with additional limitation(s) as recited in Claims.

Kawakami et al. teach a process of isolating lactoferrin using a column comprising Cellulofine™ or Chitopearl™ as shown in Examples 1-2, § 4. Kawakami et al. teach method step of applying milk to said column(s) and passing it at a rate of 10 ml/minute (equal to 600 ml/hour, see middle of Example 1, §4) and eluting lactoferrin with 1.0M aqueous sodium chloride solution. It is noted that 10 ml solution volume occupies 3.1 cm in length inside the column with 2 cm diameter, which is the column of Kawakami et al.; thus, the 10 ml/min flow rate of Kawakami et al. would translate into 3.1 cm/min flow rate inside the column of Kawakami et al. The flow rate of Kawakami et al. (i.e., 3.1cm/min = 186 cm/hour) which meets the limitation of recited "a linear flow rate of at least 1.500 cm/hour" in claim 1. Kawakami et al. specifically recites "In the present invention, the contact of the sulfuric ester with raw milk containing lactoferrin is conducted at a temperature of 50°C" (see §2, lines 40-42), which involves step of heating the milk and the column to at least 50°C. It is noted that the column of

Kawakami et al. meets the limitation of an expanded bed adsorption column which comprises an adsorbent. Thus, the purification steps of Example 1 or 2 are carried out at 50°C and the method steps of lactoferrin isolation by Kawakami et al. meet all limitations of Claims 1, 6-9 and 13-15. Because the lactoferrin is 80,000 Dalton (see Mitoma et al. Figure 2 on page 18062), the method of Kawakami et al. meets the limitation of Claim 5 reciting a bio-molecule having "at least 1000 Daltons". Hirai et al. teach a Cellulofine available from ChissoCorp. can have a particle diameter of "45 to 105  $\mu\text{m}$ "; thus, the Cellulofine™ used in the system of Kawakami et al. meets the limitation of Claims 10-12. The process of Kawakami et al. using Chitopearl™ comprises the step of loading milk on to the column and eluting lactoferrin, which meets the limitation of process of claim 1 in view of reasons stated above. Furthermore, the Chitopearl particle has a density of 390.8  $\text{kg}/\text{m}^3$  as a wet particle (see Table 1 of Yoshida et al. 1994, on page 1088). Because the particle is wet, the volume in  $\text{m}^3$  (cubic meter) would be comparable to a volume measured in ml to calculate volume, and the density of 390.8  $\text{kg}/\text{m}^3$  translates into a density of 390800 g/ml, which meets the limitation of claim 12 reciting "a density of at least 1.5 g/ml". Yoshida et al. also teach the particle size is 175  $\mu\text{m}$  (i.e., 0.504 x 248.6  $\mu\text{m}$ , see Table 1, on page 1068); thus meeting the limitation of Claim 10. Thus, a process taught by Kawakami et al. meets limitations of Claims 1, 5-10 and 12-15.

***Claim Rejections - 35 USC § 103***



The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawakami et al. (US Patent 4,997,914, Mar. 5, 1991) as evidenced by Hirai et al. (US Patent 6,475,478, Nov. 5, 2002), Mitoma et al. (The Journal of Biological Chemistry, volume 276, pages 18060-18065) and Yashida et al. (Biotechnology and Bioengineering, 1994, volume 43, pages 1087-1093).

Claim 1 is drawn to a process for isolation of one or more bio-molecule(s) from a bio-molecule containing fluid comprising the steps of: a) optionally adjusting the pH of the bio-molecule-containing fluid; b) bringing the bio-molecule-containing fluid to a temperature of at least 40°C; c) applying a volume of said bio-molecule-containing fluid having a temperature of at least 40°C to an expanded bed adsorption column comprising an adsorbent, said expanded bed column is operated with a linear flow rate of at least 1.500 cm/hour; d) optionally washing the column; e) eluting at least one bio-molecule from the adsorbent. Claims 2-15 are drawn to a process of Claim 1 with additional limitation(s) as recited in Claims.

Kawakami et al. teach a process of isolating lactoferrin using a column comprising Cellulofine™ or Chitoparl™ as shown in Examples 1-2, § 4. Kawakami et al. teach method step of applying milk to said column(s) and passing it at a rate of 10 ml/minute (equal to 600 ml/hour, see middle of Example 1, §4) and eluting lactoferrin

with 1.0M aqueous sodium chloride solution. It is noted that 10 ml solution volume occupies 3.1 cm in length inside the column with 2 cm diameter, which is the column of Kawakami et al.; thus, the 10 ml/min flow rate of Kawakami et al. would translate into 3.1 cm/min flow rate inside the column of Kawakami et al. The flow rate of Kawakami et al. (i.e., 3.1cm/min = 186 cm/hour) which meets the limitation of recited "a linear flow rate of at least 1.500 cm/hour" in claim 1. Kawakami et al. specifically recites "In the present invention, the contact of the sulfuric ester with raw milk containing lactoferrin is conducted at a temperature of 50°C" (see §2, lines 40-42), which involves step of heating the milk and the column to at least 50°C. It is noted that the column of Kawakami et al. meets the limitation of an expanded bed adsorption column which comprises an adsorbent. Thus, the purification steps of Example 1 or 2 are carried out at 50°C and the method steps of lactoferrin isolation by Kawakami et al. meet all limitations of Claims 1, 6-9 and 13-15. Because the lactoferrin is 80,000 Dalton (see Mitoma et al. Figure 2 on page 18062), the method of Kawakami et al. meets the limitation of Claim 5 reciting a bio-molecule having "at least 1000 Daltons". Hirai et al. teach a Cellulofine available from ChissoCorp. can have a particle diameter of "45 to 105 um"; thus, the Cellulofine™ used in the system of Kawakami et al. meets the limitation of Claims 10-12. The process of Kawakami et al. using Chitopearl™ comprises the step of loading milk on to the column and eluting lactoferrin, which meets the limitation of process of claim 1 in view of reasons stated above. Furthermore, the Chitopearl particle has a density of 390.8 kg/m<sup>3</sup> as a wet particle (see Table 1 of Yoshida et al. 1994, on page 1088). Because the particle is wet, the volume in m<sup>3</sup>

(cubic meter) would be comparable to a volume measured in ml to calculate volume, and the density of 390.8 kg/m<sup>3</sup> translates into a density of 390800 g/ml, which meets the limitation of claim 12 reciting "a density of at least 1.5 g/ml". Yoshida et al. also teach the particle size is 175  $\mu$ m (i.e., 0.504 x 248.6  $\mu$ m, see Table 1, on page 1068); thus meeting the limitation of Claim 10. Thus, a process taught by Kawakami et al. meets limitations of Claims 1, 5-10 and 12-15.

Kawakami et al. do not teach a process for isolation of a bio-molecule from a bio-molecule containing fluid comprising an expanded bed column that is a large-scale column has at least 10 liter of sedimented adsorbent, has about 50 to 100 liter of sedimented adsorbent or has a diameter of at least 10 cm.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to scale up the size of column to an industrial scale for the production of isolated lactoferrin using the process of Kawakami et al., wherein the industrial scaled column would meet the size and/or the volume as disclosed in Claims 2-3 because "lactoferrin is an iron-binding glycoprotein present in an exocrine liquid such as milk and has a variety of physiological activities such as bacteriostasis against pathogenic bacteria, adjusting function of leukocyte differentiation, build-up function of germicidal power, multiplicative function of lymphocyte and adjusting function of iron absorption" (see §1, lines 13-14) and Kawakami et al. specifically recites the method described above in 35 USC 102/103 is preferred method in industrial scale because other column such as agarose is soft, which is liable to deforming (see §2, lines 18-22) and cause it to decrease the flow rate (see top of right column of Yoshida et al.).

Accordingly, one skilled in the art would have been motivated to use industrial scaled column using the process of Kawakami et al. as described above; thus, the invention taken as a whole is *prima facie* obvious.

***Conclusion***

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEXANDER D. KIM whose telephone number is (571)272-5266. The examiner can normally be reached on 11AM-7:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on (571) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Alexander D Kim/  
Examiner, Art Unit 1656

/Richard G Hutson, Ph.D./  
Primary Examiner, Art Unit 1652